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Hematologic aspects of cardiotomy suction in cardiac operations

Although membrane oxygenators (MO's) instead of bubble oxygenators (BO's) have been introduced in cardiac operations, substantial improvements in hemocompatibility have not yet been obtained. Intensive blood/air contact during cardiotomy suction is considered to be a remaining major destructive factor. A suction system with a blood level detector and an electronic circuit regulating the pump speed has been developed to eliminate intensive blood/air contact. This study quantitates the improvement that can be obtained when controlled suction is used in combination with an MO in cardiac operations. In canine experiments thrombocyte numbers and function, bleeding times, plasma hemoglobin levels, erythrocyte numbers, leukocyte numbers, and fibrin formation were determined in the following series: I, MO (n = 6); II, MO + controlled suction (n = 6); III, MO + low-vacuum suction, blood/air = 400:300 (n = 6); IV, MO + high-vacuum suction, blood/air = 400:1,000 (n = 4). In the MO + high-vacuum suction series of experiments strongly impaired values were measured for numbers and function of thrombocytes, erythrocytes, bleeding times, and fibrin formation. On the other hand, in the MO and controlled suction series the values of these parameters remained significantly better. Low-vacuum suction yielded results in between those of MO and high-vacuum suction. Leukocyte numbers showed identical courses in all series. Conclusion: suction definitely is a noxious link in the ECC chain. It is necessary to combine the MO with controlled suction in order to minimize the damage to blood elements and so to maintain optimal hemostasis.

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For many years there has been a constant search for improvements in the oxygenator design for cardiac operations. The principles of exposing a blood film to oxygen, of bubbling oxygen through blood, and of diffusing oxygen through membranes in contact with blood have all been employed. The simplest principle, the bubble oxygenator (BO), has gained the widest application, because this design was suitable for mass production and could be delivered as a disposable item at a relatively low price. However, it was recognized that the BO with its direct blood/gas contact was a weak link in the chain of components of an extracorporeal circuit as far as hematologic damage is concerned.

The attempts to perform long-term extracorporeal circulation in patients with respiratory failure made the membrane lung with superior hemocompatibility available. The next step was to raise the effectiveness of the membrane oxygenator (MO) in order to render total bypass, needed for cardiac operation, possible. The introduction of microporous membranes instead of thin silicone rubber membranes, which are hard to produce, was a breakthrough, which made these MO's more suitable for mass production. In addition gas transfer rates, especially for CO_2, were considerably higher for these membranes.

At this moment two models, one with a microporous membrane and the other with a silicone rubber membrane, have passed the experimental stage and are readily available for clinical use. In several centers ample experience has been obtained in routine cardiac operations and prices have become competitive with those of the more sophisticated BO's. However, the complete move to the exclusive use of MO's with their superior hemocompatibility has not yet been made.

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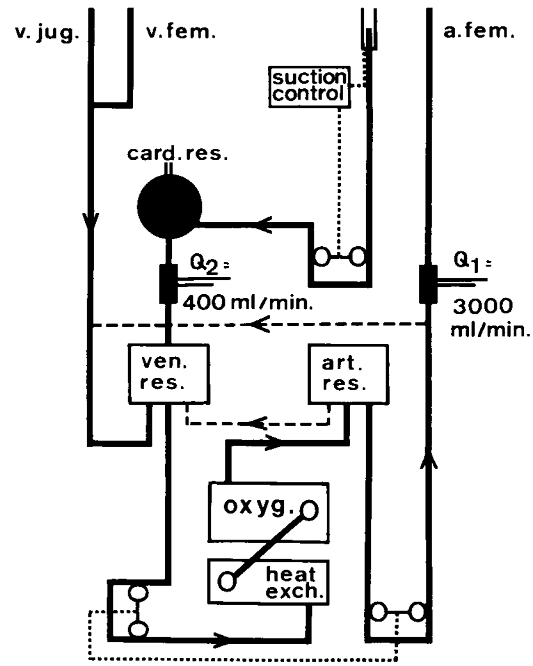

Fig. 1. Schematic presentation of the experimental setup, consisting of polyvinyl chloride tubing, roller pumps, heat exchanger, oxygenator, and cardiotomy suction system.

This is mainly because there is still another weak link in the chain of the extracorporeal circuit: cardiotomy suction acts as a vigorous blood/air contact and the relevance of using a membrane lung in such a circuit remains dubious, unless the damaging effect of suction can be eliminated.

The availability of an electronically controlled suction system which prevents suction of air and blood has enabled us to investigate quantitatively the contribution of cardiotomy suction to the hematologic damage during total bypass in canine experiments.

Materials and methods

Mongrel dogs weighing about 30 kg were premedicated with 0.5 mg of atropine sulfate and 50 mg of pethidine HCl. Anesthesia was effected with sodium pentothiobarbital (30 mg/kg of body weight intravenously) and continued with halothane (Fluothane) 0.5% in a gas mixture of nitrous oxide 4 L/min and oxygen 2 L/min after tracheal intubation. The right femoral artery and vein and the external jugular vein were cannulated and connected to an extracorporeal circuit (ECC) in a venoarterial shunt. The experimental setup of the ECC (Fig. 1) was composed of a PVC tubing system with two buffer reservoirs (Travenol Laboratories, Deerfield, Ill.), two coupled nonocclusive roller pumps (Dreissen, type Modul pump, Hellevoetsluis, The Netherlands), a heat exchanger (Travenol), and a membrane oxygenator (Travenol Modulung–Teflo 2.25 m^2). An extravascular flow probe (E.M.F. Transflow 600, Skalar, Delft, The Netherlands) was included to maintain a blood flow of 3,000 ml/min for 2 hours.

The ECC was primed with equal volumes of heparinized donor blood and gelatin plasma expander (Haemaccel). The priming volume for the ECC with MO was 3 L; during perfusion a gas flow of 5 to 6 L/min (O_2:CO_2 = 95:5) through the MO was needed to ensure physiological blood gas levels in the animal. During the experiments systemic heparinization was employed (200 IU/kg of body weight initially and 100 IU/kg every hour) and neutralized by protamine chloride (2 mg/kg) after disconnection of the ECC.

Thoracotomy was performed in those animals in which cardiotomy suction was included in the ECC. Both venae cavae were snared and, after electrically induced fibrillation of the heart, both atria were incised. Blood was aspirated from a pericardial well through a silicone rubber tubing system with a roller pump (Sarns Inc., type 6013, Ann Arbor, Mich.) and a cardiotomy reservoir (Bentley ATS unit 100). A flow probe was interconnected in the system to determine the amount of suction (average suction 400 ml/min). Three modes of suction were standardized. The commonly used suction with high vacuum was defined by the ratio 400 ml/min of blood: 1,000 ml/min of air (high-vacuum suction), which was measured with a purgemeter (Brooks-Mite DSE 2000, Hatfield, England). Manual adaptation of the suction capacity to the loss of blood was quantitated in the ratio 400:300 (low-vacuum suction). The optimal adaptation of cardiotomy suction was reached by an electronically regulated suction system[1] in which air suction was virtually eliminated (ratio 400:0—controlled suction). In this system the pump speed is regulated according to the blood level in the pericardial well. This level is sensed by two titanium electrodes coated with titanium oxide which are located above the sucker tip. These electrodes are supplied with a high-frequency voltage. The current through the circuit is linearly dependent on the blood level. This signal serves as input for a regulating device, attuned to the specific aims of cardiotomy suction. The suction pump is driven by this regulating device. The blood level regulating device (Medical Scientific Application, Den Bosch, The Netherlands) prevents suction of air by maintaining the sucker tip below the blood level. Cardiotomy suction was instituted after 30 minutes of ECC for a period of 1 hour.

The following experiments were performed: I, Teflo

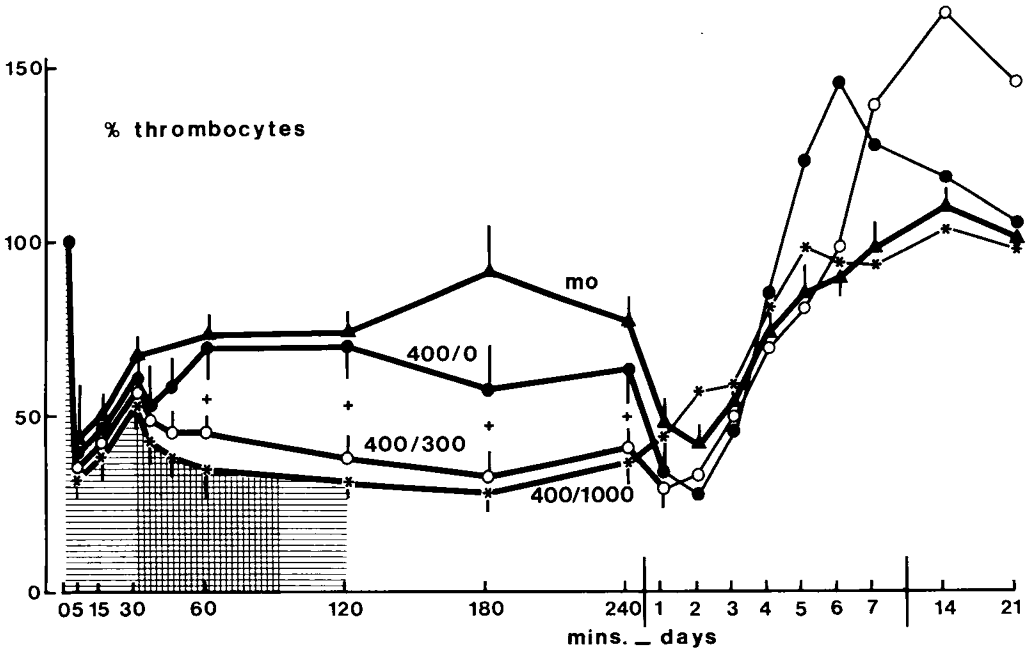

Fig. 2. Mean values and standard errors of the number of circulating thrombocytes, as related to the preoperative values, during and after extracorporeal circulation (ECC) with a membrane oxygenator *(MO)*, MO + controlled suction, MD + low-vacuum suction (blood/air = 400:300), and MO + high-vacuum suction (blood/air = 400:1,000). Statistically significant differences ($p < 0.05$) between the groups are marked with an *asterisk*.

MO, n = 6; II, Teflo MO + suction blood:air = 400:0 (controlled suction), n = 6; III, Teflo MO + suction blood:air = 400:300 (low-vacuum suction), n = 6; IV, Teflo MO + suction blood:air = 400:1,000 (high-vacuum suction), n = 4.

Blood samples were taken from an indwelling catheter in the left femoral artery: before cannulation and after 5, 15, 30, 60, and 120 minutes (in addition, after 35 and 45 minutes in the suction groups) during ECC; after 60 and 120 minutes after ECC, and, by means of venipuncture, daily in the recovery period during the first week, on day 14, and on day 21. Only hematologically normal dogs were used for the experiments. Thrombocytes, leukocytes, and erythrocytes were counted with an automatic cell counter (Coulter Counter, Dunstable, England) calibrated for canine blood cells. Adenosine diphosphate (ADP)-induced thrombocyte aggregation was performed by means of an adapted Born[2] technique and expressed by the maximal optical density loss (OD_{max}). Bleeding times were determined in the upper hind leg according to a modified method of Borchgrevink and Waaler.[3] Standard laboratory techniques were used to measure hemoglobin, hematocrit, SRE,[4] fibrinogen,[5] prothrombin time (PT),[6] activated partial thromboplastin time (APTT),[7] thrombin time,[8] and reptilase time.[9] Plasma hemoglobin levels were determined by means of the method of Lee Kum Tatt and Ai-Mee Ling.[10] Cellular counts, thrombocyte aggregations, hematocrits, and hemoglobin levels are expressed as percentages of the preoperative values. To eliminate the effect of hemodilution caused by the priming of the ECC, cell counts, fibrinogen, and plasma hemoglobin levels were corrected for changes in hematocrit on the day of the experiment. For thrombocyte counts under 80×10^9 L the ADP-induced aggregation was corrected according to a nomogram as previously described.[11]

Statistical analysis of the results included Student's t test for two means and Student's paired t test.

Results

In Group I (MO), in which extracorporeal circulation was performed without thoracotomy, all dogs survived during the whole experimental period of 3 weeks. In contrast, in Groups II to IV, in which thoracotomy was needed to allow cardiotomy suction, a high incidence of lethal hematothorax was experienced after postoperative day 1 (Group II, 3/6; Group III, 4/6; Group IV, 2/4). However, on postoperative day 1 sufficient survivals remained in each group to permit statistical comparison (Group II, 5/6; Group III, 4/6; Group IV, 2/4). The data of the few surviving dogs in the suction

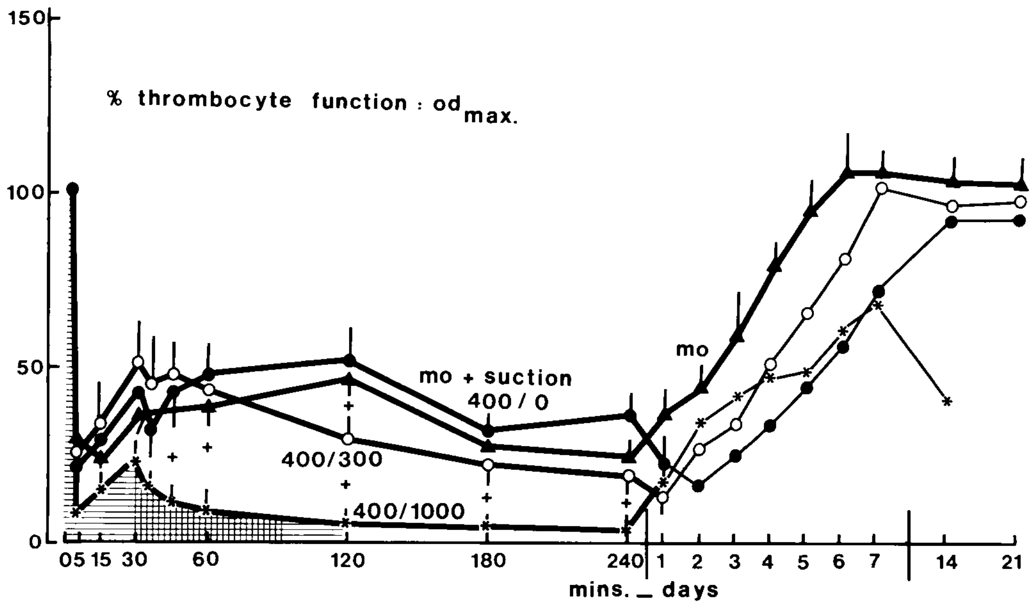

Fig. 3. Mean values and standard errors of maximal optical density loss (OD_{max}) of ADP-induced thrombocyte aggregation, as related to the preoperative values, during and after ECC with an MO, MO + controlled suction, MO + low-vacuum suction (blood/air = 400:300), and MO + high-vacuum suction (blood/air = 400:1,000). Statistically significant differences ($p < 0.05$) between the groups are marked with an *asterisk*.

groups during the following period are given only to show trends of recovery.

The number of circulating thrombocytes. In all series this number showed an immediate and sharp drop to a value of 26% (Fig. 2) after the initiation of ECC. This percentage corresponds to about 55×10^9 thrombocytes per liter. After this pronounced initial dip a rapid recovery was seen within 30 minutes and in the series without suction the number of circulating thrombocytes stabilized at a level of around 72% for the remaining period of ECC. After disconnecton of the ECC numbers increased to 92% with a gradual decrease thereafter to a secondary dip of 42% on day 2. The initiation of cardiotomy suction after 30 minutes of perfusion was clearly reflected in consequent decreases in the number of circulating thrombocytes (Fig. 2). This decrease was persistent in the groups with high- and low-vacuum suction, but transient in the group with controlled suction. In the latter group the curve followed the pattern of the first series without suction and numbers stabilized at about 70%. In contrast, the curve of the group with high-vacuum suction stabilized at about 30% during the day of experiment. The group with low-vacuum suction showed a low level of thrombocyte numbers similar to that of the high-vacuum suction group. The few long-term surviving animals in both the controlled suction and the low-vacuum suction groups showed an overshoot to about 150% thrombocytes on days 6 and 14, respectively.

Thrombocyte function. This function, as expressed by the OD_{max} of the ADP-induced aggregation, decreased to 22% immediately after the initiation of ECC in the group of MO experiments without suction (Fig. 3), but recovered to 47% at the end of the bypass period. After disconnection OD_{max} decreased to a minimal value of 22% after 240 minutes. During the postoperative days OD_{max} increased gradually and stabilized at about 100% from day 6 onward. When suction was instituted, a pattern was observed similar to that for thrombocyte numbers: persistent drops in both vacuum suction groups in contrast to a transient drop in the group with controlled suction. The latter group again followed the course of the MO series without suction, whereas in the high-vacuum suction group the OD_{max} was virtually absent from 60 minutes onward until the end of the day of experiment. The curve of the low-vacuum suction group tended to follow the MO curve without suction.

Fibrin formation. At the end of the day of experiment the MO, the controlled suction, and the low-vacuum suction groups showed normal values for the APTT, PT, and reptilase time (RT) (Fig. 4). Thrombin time was slightly prolonged in the suction series. Fibrinogen showed normal levels in the MO series, but

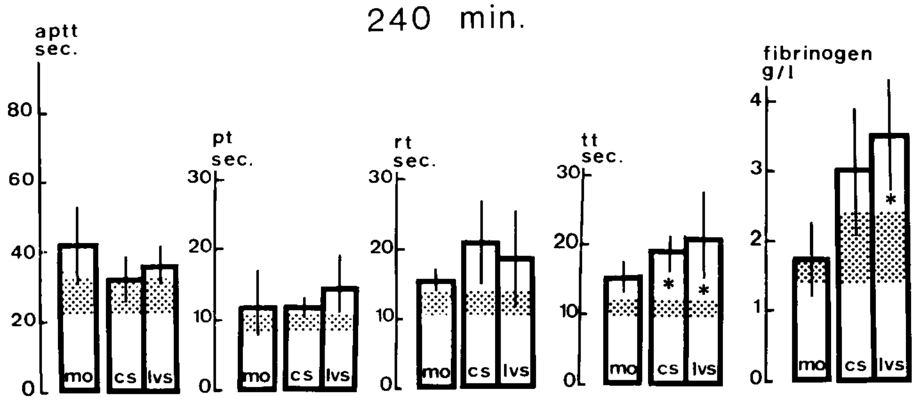

Fig. 4. Mean values and standard errors of the parameters of fibrin formation after (240 minutes) ECC with an MO, MO + controlled suction *(cs)*, and MO + low-vacuum suction *(lvs)* (blood/air = 400:300). The activated partial thromboplastin time *(aptt)*, the prothrombin time *(pt)*, the reptilase time *(rt)*, the thrombin time *(tt)*, and the fibrinogen concentration are given. Statistically significant abnormal values ($p < 0.05$) are marked with an *asterisk*.

had increased to concentrations of 3 to 3.5 gm/L in the suction series. Significant differences could be distinguished only between the MO and the low-vacuum suction series for the increase in fibrinogen concentration.

Fibrin formation as well as plasma hemoglobin levels have not been measured in the high-vacuum suction series.

Bleeding times. After 240 minutes bleeding times were severely prolonged to values of over 15 minutes in the MO group with high-vacuum suction (Fig. 5). In contrast, the bleeding times were only slightly prolonged in the MO group as well as in the MO group with controlled suction. In the group of MO with low-vacuum suction, values were in between these two extremes. On postoperative day 1 shortenings of the bleeding times were measured, but the distinctions between the groups remained highly significant. In the few surviving dogs of the suction series the bleeding times normalized during the further postoperative period.

The erythrocyte damage in the different groups showed the same general pattern (Fig. 6) as the other parameters.

Plasma hemoglobin levels. These levels did not change in an ECC with an MO during the first 15 minutes. When suction was instituted, plasma hemoglobin levels increased. At the end of the perfusion period significant differences were present between the groups. The controlled suction group (24 μmol/L) showed small but significant differences as compared to the MO groups without suction (9 μmol/L); the MO

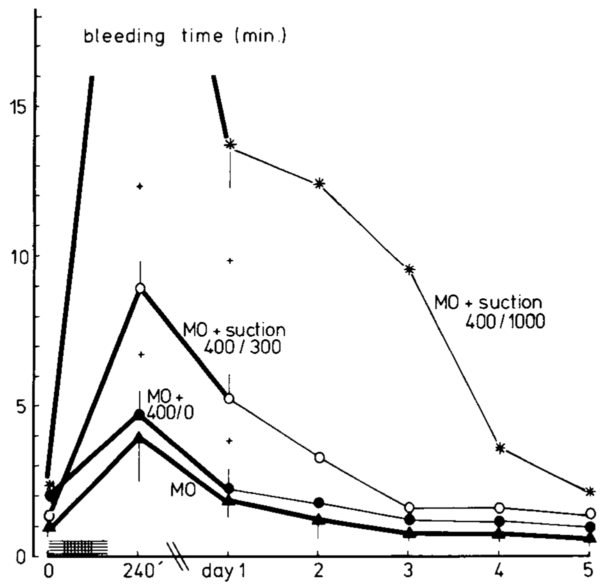

Fig. 5. Mean values and standard errors of the bleeding times before and after ECC with an MO, MO + controlled suction, MO + low-vacuum suction (blood/air = 400:300), and MO + high-vacuum suction (blood/air = 400:1,000). Statistically significant differences ($p < 0.05$) between the groups are marked with an *asterisk*.

group with low-vacuum suction (54 μmol/L) had significantly higher levels than the controlled suction group (24 μmol/L). In the postoperative period plasma hemoglobin levels decreased; in all surviving animals normal levels were measured on day 2.

Erythrocyte numbers. Only minor changes in these numbers could be seen during the day of experiment. In

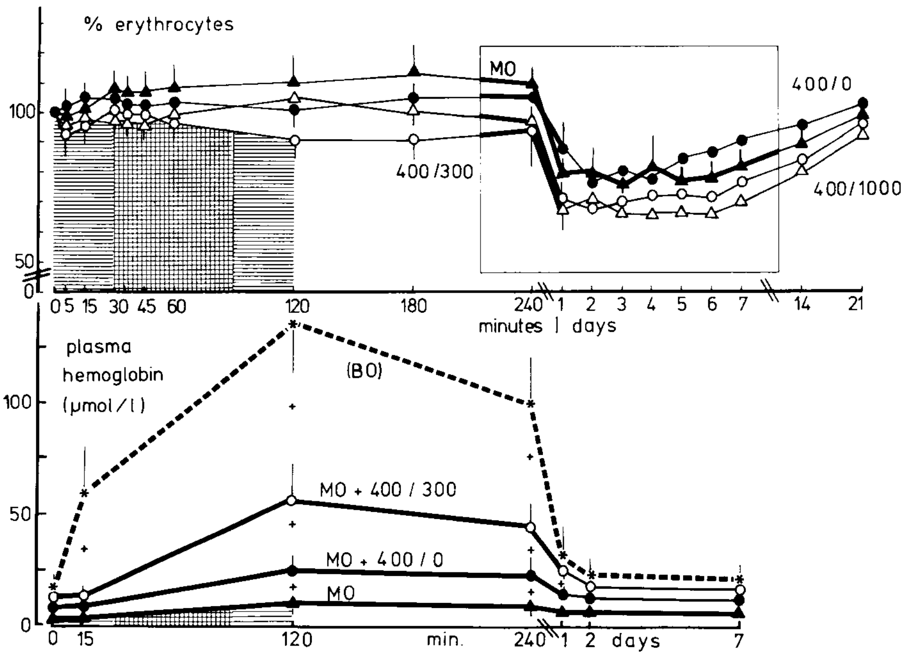

Fig. 6. Mean values and standard errors of erythrocytes, related to preoperative numbers, and plasma hemoglobin levels before, during, and after ECC with an MO, MO + controlled suction, MO + low-vacuum suction (blood/air = 400:300), and MO + high-vacuum suction (blood/air = 400:1,000). For reasons of comparison plasma hemoglobin concentrations during and after bubble oxygenator *(BO)* experiments are added to the figure.[39] Statistically significant differences ($p < 0.05$) between the groups are marked with an *asterisk*.

the MO and the controlled suction groups slightly increased levels of about 100 to 110% were measured, whereas both vacuum suction groups showed somewhat decreased levels of about 90 to 100%. More important changes were observed on postoperative day 1. The lowest levels (about 65%) were seen in the MO/high-vacuum suction group. The MO and controlled suction groups resulted in significantly less decreased erythrocyte numbers (80 to 85%) and the low-vacuum suction group showed intermediate values. In the surviving animals normal preoperative erythrocyte numbers were found after 3 weeks.

Leukocyte numbers. These numbers showed similar changes in all groups. A rapid leukocytosis with a maximum of about 300% on postoperative day 1 was followed by a gradual decrease to values around 150% on day 4; a second maximum of about 250% appeared around day 6. In the high-vacuum suction group this second maximum showed a higher value of about 350%. Normal values were measured after 2 weeks.

Discussion

For some years it has been recognized that BO's, roller pumps and the nonphysiological materials of the ECC may be held responsible for the manifold complications experienced in patients after cardiac operations. Continuously, severe hemorrhages,[12-15] infections,[16-19] and anemia[20, 21] are reported in both clinical and experimental circumstances. We have shown before that a careful choice of pumps and materials yields some hematologic advantages.[11] More substantial improvements were obtained experimentally by the use of an MO instead of a BO: postoperative hemorrhages were greatly reduced[11, 22] and hemolysis was virtually eliminated.[23, 24] Yet these improvements, obtained in well-defined experimental circumstances, could not be achieved in the more complex clinical situation. This is most likely due to the fact that the blood damage, brought about by cardiotomy suction, interferes with the improved hemocompatibility of the MO.[21, 25] Therefore, as reported by Hill[26] and others,[27] the MO does not offer significant hematologic benefits to the patient in clinical circumstances. Siderys and coworkers[23] have shown that the use of an MO did show superior results when the blood of cardiotomy suction was discarded. However, this alternative might give rise to logistic problems for blood supply in large centers. We have tried to exclude the cause of damage to the blood during cardiotomy suction by preventing suction of blood and air by means of an electronically controlled suction system.[1]

Thrombocyte numbers. The experimental ECC procedures, performed in dogs under identical and strictly standardized circumstances, show common patterns in all four series of experiments. In accord with the observations of other investigators[12, 28, 29] an immediate and sharp decrease in thrombocyte numbers after starting ECC was found (Fig. 2). This instantaneous massive disappearance of thrombocytes from the circulation must be explained by an acute intravascular aggregation phenomenon induced by released bioamines or serotonin from affected blood elements.[11] Elevated serotonin and ADP concentrations during ECC have been reported by others.[29-31] However, this initial dip might also be induced or aggravated when plasma expanders with an apparent aggregating effect[32] are used in the priming solution. This aggregation process appears to be partly reversible and the stable level after half an hour suggests an equilibrium between aggregation and consequent disaggregation of the thrombocytes. The high level of numbers is indicative of the superior hemocompatibility of an MO as compared to a BO.[11] After the disconnection of the ECC the equilibrium of aggregation and disaggregation is interrupted in favor of disaggregation. However, after a temporary increase in numbers, a secondary dip appears on the second day. This can be explained by the early elimination of damaged thrombocytes from the circulation.[33] Such a secondary dip is also seen after BO experiments[11] but, because numbers are much lower during the stable phase, this results in an almost complete loss of circulating thrombocytes, an observation also made by others.[15, 34] When the formation of new thrombocytes exceeds the elimination of affected thrombocytes, the resulting gradual restoration toward normal values occurs in about 1 week.[34] This period of thrombocytopenia after ECC is in accordance with the reports of Moriau and co-workers[29] and McKenzie and co-workers,[35] who observed periods of thrombocytopenia of 3 and 6 days, respectively.

Thrombocyte function. Several investigators have reported depressed thrombocyte function during ECC.[12, 13, 15, 29, 36, 37] In our experiments with the MO, thrombocyte function shows a pattern comparable to that of thrombocyte numbers: an initial dip and stabilization after half an hour. Postoperatively also a clear onset of restoration is observed from day 2, parallel to the increase in thrombocyte numbers, and a normal thrombocyte function is measured on day 5.

The use of an MO in combination with different modes of cardiotomy suction results in clear differences. In the actual clinical situation, in which high-vacuum suction is mostly applied, both thrombocyte numbers and function will be drastically decreased. Most impressive is the complete loss of function in the high-vacuum suction experiments. Practically, the potential benefits of an MO are completely eliminated by the cardiotomy suction. Careful use of vacuum suction might give some improvement, as is shown by a better maintained thrombocyte function during the day of experiment. The introduction of the controlled suction system permits elimination of blood/air contact in the suction line; this clearly results in a decrease in damage to the thrombocytes: numbers and functions are equally preserved as in the MO group without suction. So on the day of experiment no evident additional damage to the thrombocytes is introduced by controlled suction. On postoperative day 1 differences between the groups have mostly disappeared because of a more delayed elimination of affected thrombocytes in the MO and controlled suction series.

Fibrin formation. The results of the coagulation parameters show that fibrin formation plays an additional but minor role in the process of ECC-induced hemostatic disturbances; no important abnormalities can be observed. Hyperfibrinogenemia in the suction groups must be considered as a reaction to the performed thoracotomy[14, 38] and not as a result of the suction procedures per se.

Bleeding time. The bleeding time is affected by the combination of changes in thrombocyte numbers and function and, to a lesser extent, by fibrin formation. Consequently the bleeding time is of great practical relevance as an over-all measurement of hemostasis, although the parameter is neither very accurate nor very sensitive. In spite of this, the results of the bleeding time measurements in our experiments are consistent with the thrombocyte behavior in the various groups. On the one hand they clearly show the potential beneficial effects of the use of an MO, but on the other hand they demonstrate the deleterious effect of the high-vacuum cardiotomy suction, which eliminates whatever profit has been gained. Low-vacuum suction also induces increased bleeding risks, though less pronounced as compared with high-vacuum suction. The benefits of the controlled suction system are accentuated by the possibility of maintaining approximately normal bleeding times.

Plasma hemoglobin. The differences in damage to the erythrocytes, observed in the four groups, emphasize the observations made in the differences in thrombocytes and bleeding time. The maximum levels of plasma hemoglobin reached at the end of the perfusion show the same grouping as has been observed for the thrombocyte damage. We have shown before that maximal plasma hemoglobin levels in BO perfusion are 15 times the level in MO perfusion.[39] Low-vacuum suction produces six times more hemolysis than MO perfusion without suction. The minor though significant differences between the MO and the controlled suction experiments may be due to mesothelial surface contact[40] as well as to an additional damaging effect of the suction circuit. The plasma hemoglobin levels measured in our experiments are in accordance with the observations made by other investigators: Murphy and associates[38] reported maximal plasma hemoglobin levels of 18 μmol/L in MO perfusion, whereas Siderys and colleagues[23] measured about 200 μmol/L during suction of blood. Other investigators[25, 27, 41] did not distinguish any differences between MO and BO when high-vacuum suction was combined with MO. Postoperatively the parameter of plasma hemoglobin is not an exact measure for the degree of hemolysis because free hemoglobin is bound as dissociated dimers to haptoglobin,[42] as oxidized heme groups to hemopexin,[43] or eliminated by renal filtration.

Erythrocyte numbers. In the postoperative period a better indication of the erythrocyte damage can be obtained from the erythrocyte numbers. The acute effect of hemodilution on erythrocyte numbers has been corrected during the day of experiment according to the changes in the hematocrit and is therefore not reflected in the presented curves. During perfusion no major changes in these corrected values are observed in the different groups. A tendency toward a small increase is seen in the MO and controlled suction groups, whereas minor decreases are measured in the vacuum suction groups. As is shown by increased plasma hemoglobin levels in the latter groups, a substantial decrease of erythrocyte numbers is to be expected. The normal values indicate that these losses of erythrocytes during perfusion have most likely been compensated by spleen contraction. The development of severe postoperative anemia substantiates the reports of erythrocyte damage during ECC.[44-47] The postoperative anemia, due to the elimination of erythrocytes damaged during ECC, shows the same pattern in the four groups as the other parameters do: on postoperative day 1 controlled suction is in the range of MO perfusion, whereas high-vacuum suction shows much lower values.

Leukocyte numbers. No essential differences between the groups are observed in the courses of leukocyte numbers. The rapid leukocytosis to a maximum of 300% points to a quick release of leukocytes from the reservoir of the marginating pool into the circulation. Moreover, leukopoiesis is a fast process and both mechanisms can easily compensate for leukocyte destruction in the ECC. Only longer lasting perfusion periods can be expected to exhaust the large leukocyte reservoirs. The curves with ''camel-humps'' on days 1 and 4 can be explained by superimposed curves of rapid leukocyte elimination and formation. The dip in between might be the result of depletion of the marginating pool. More indicative of the damage to the leukocytes and the consequences for the patient's defense mechanism against bacterial infection would be the assessment of the function of the neutrophilic leukocytes. A recently applied simple technique of carbonyl-iron phagocytosis[48] has been useful to show the effects of ECC components on leukocyte function. It has also illustrated the correlation between a decreased leukocyte function and a higher susceptibility to infection.[49] More extensive studies with this technique are now envisaged in order to elucidate the factors responsible for the reported relatively high infection rates after a cardiac operation.[16, 17, 18, 50]

The results of our experiments accentuate the fact that in today's setup with uncontrolled cardiotomy suction, there is little relevance in using an MO instead of the hematologically more aggressive BO; all benefits gained by using the MO are counteracted by the suction. The hemocompatibility of cardiotomy suction can be improved, as has been demonstrated by the results in our controlled suction group. Only when this controlled suction system can be introduced in the routine cardiac operation is definite improvement of hemocompatibility to be expected from the use of an MO.

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